

Award Number: W81XWH-14-2-0183

TITLE: Prostate Cancer Biorepository Network (PCBN)

PRINCIPAL INVESTIGATOR: Colm Morrissey

CONTRACTING ORGANIZATION: University of Washington
Seattle, WA 98195-6510

REPORT DATE: October 2017

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release; Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

*Form Approved
OMB No. 0704-0188*

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. **PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.**

1. REPORT DATE October 2017			2. REPORT TYPE Annual		3. DATES COVERED 09/30/2016 - 09/29/2017	
4. TITLE AND SUBTITLE Prostate Cancer Biorepository Network (PCBN)					5a. CONTRACT NUMBER	
					5b. GRANT NUMBER W81XWH-14-2-0183	
					5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Colm Morrissey PhD					5d. PROJECT NUMBER	
E-Mail: cmorriess@uw.edu					5e. TASK NUMBER	
					5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) University of Washington 4333 Brooklyn Ave Seattle WA 98195-0001					8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012					10. SPONSOR/MONITOR'S ACRONYM(S)	
					11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited						
13. SUPPLEMENTARY NOTES						
14. ABSTRACT The Genitourinary Cancer Biorepository at the University of Washington joined the Prostate Cancer Pathology Resource Network (PCBN) September 30 th 2014. The purpose of this interaction is to provide high quality, well annotated specimens that can be used by prostate cancer researchers through the PCBN. The University of Washington Biorepository has a focus on advanced stage disease. Specimens provided by the University of Washington site includes blood (serum, plasma, and buffy coat), prostatectomy tissues (frozen), biopsies and metastatic tissue from rapid autopsies (paraffin embedded material and tissue microarrays (TMAs)), prostate cancer patient derived xenografts (PDX) and derived specimens (DNA and RNA) from prostate cancer patients. These specimens are linked to clinical and outcome data and supported by an informatics infrastructure. In this 2 nd year of operation the University of Washington site has accrued new specimens from the clinic, surgery, and at autopsy, manufactured and provided TMAs, sera and derived RNA and DNA where required. Specimens were made available to prostate cancer researchers through the PCBN.						
15. SUBJECT TERMS Biorepository, prostatectomy, rapid autopsy, patient derived xenografts						
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT Unclassified	18. NUMBER OF PAGES 6	19a. NAME OF RESPONSIBLE PERSON USAMRMC	
a. REPORT Unclassified					19b. TELEPHONE NUMBER (include area code)	
b. ABSTRACT Unclassified			c. THIS PAGE Unclassified			

Table of Contents

	<u>Page</u>
1. Introduction.....	3
2. Keywords.....	3
3. Accomplishments.....	3
4. Impact.....	4
5. Changes/Problems.....	4
6. Products.....	5
7. Participants & other Collaborating Organizations.....	5
8. Special Reporting Requirements.....	5
9. Appendices.....	5

Introduction

The Prostate Cancer Biorepository Network (PCBN) is a public bioresource that provides high quality, well annotated specimens that can be used by prostate cancer researchers through the PCBN <http://prostatebiorepository.org>. This biorepository is a collaborative effort between Johns Hopkins University (JHU), New York University (NYU), Memorial Sloan Kettering Cancer Center (MSKCC), University of Washington (UW), Washington University (WU), and the Department of Defense. The PCBN coordinating center is at JHU. UW is a network site.

The Genitourinary Cancer Biorepository at the University of Washington joined the Prostate Cancer Pathology Resource Network (PCBN) September 30th 2014. The UW Prostate Cancer Program has for over 25 years collected and distributed biospecimens to investigators worldwide. During that time the University of Washington Biorepository has focused on advanced stage disease. Access to clinical specimens from patients with advanced disease can be challenging so the Genitourinary Cancer Biorepository set up a rapid autopsy program to provide access to metastatic tissue and create patient derived xenograft (PDX) models of advanced disease. The biorepository also has an extensive collection of blood (serum, plasma, and buffy coat), prostatectomy tissues (frozen), and derived specimens (DNA and RNA) from prostate cancer patients; these specimens are linked to clinical and outcome data and supported by an informatics infrastructure.

Keywords

Biorepository, prostate cancer, patient derived xenografts, rapid autopsy, biomarkers.

Accomplishments

The Major goals of the project were (1) patient accrual and biospecimen acquisition, (2) providing specimens to external investigators, and (3) improving biospecimen science.

Patient Accrual and Biospecimen Acquisition:

The adjacent table shows specimens prospectively accrued to the PCBN through the University of Washington during the 12 month period covered by this report. Similar to last year, African American patients comprised only 2% of the patient specimens we accrued at UW. Increasing enrollment is an ongoing challenge for investigators at UW.

Biospecimen Acquisition October 2016 - September 2017	Total Specimens Collected
Serum	
Pre-RRP	78
Metastatic	38
Total	116
Tissue	
Prostatectomy	79
Metastatic Sites Sampled	168
Normal Sites Sampled	172
Metastatic Biopsy	0
Total	419

Radical prostatectomies: During the year we prepared frozen OCT embedded tissues from 79 prostatectomies. Twenty-three were from high risk patients (Gleason 8 and above), 49 were from medium risk (Gleason 7) and 7 were low risk (Gleason 6).

Rapid autopsies: We performed fifteen rapid autopsies during the last year. The prostate cancer patients are approached by oncologists in the clinic and through the altruism and generosity of the patients and their families as soon as the patient passes we dispatch an ambulance to pick up the body and bring it back to the University of Washington where our autopsy team is prepared for a rapid autopsy and tissue acquisition. Based on our

historic data we typically expect 8 autopsies a year and we have performed 15 in the last year. All specimens have been processed and read by a pathologist.

Serum and Plasma Isolation: Sera were obtained from 78 prostatectomy patients and 38 metastatic patients. Plasma and buffy coats were obtained from 76 prostatectomy patients and 1 metastatic patient.

Metastatic Biopsies: We have obtained paraffin embedded metastatic biopsies from 0 patients. No oligo metastases or biopsies were available to the Biorepository for collection.

Tissue Microarrays: We have manufactured a tissue microarray (TMA) with 42 LuCaP PDX models with different characteristics. Includes neuroendocrine lines, castration resistant lines and androgen sensitive lines - 3 cores from 3 xenografts from each line, across 4 blocks. We are currently manufacturing a new metastasis TMA that will include specimens from 2012 to date.

Patient Derived Xenografts: One new line 'LuCaP 208' has been established this year based on the premise of the lines passaging over 3 times as xenografts in animals with continuous growth. We are currently maintaining 42 lines and continue to passage tumors in animals to develop new lines.

DNA/RNA Isolation: We have a bank of RNA/DNA from primary prostate, xenografts and metastases, but as we collect more tissue we isolate additional RNA and DNA. This year RNA was isolated from a further 61 xenograft tumors, and 42 additional metastases.

Providing Specimens to External Investigators:

We have provided serum samples from 46 patients with CRPC. Paraffin embedded sections from 53 CRPC patients (3 sections/patient) and 6 patients with primary disease. Additionally, we provided paraffin embedded sections from 6 neuroendocrine metastases, 3 LuCaP xenograft lines, and normal prostate (16 sections/patient). We provided frozen tissue from 48 LuCaP xenografts and 4 primary prostates. We also sent out 17 LuCaP xenograft TMAs and 5 metastasis TMAs. Finally, we also sent out matched RNA and DNA from 5 LuCaP xenograft lines and 10 metastases. All specimens were provided with associated de-identified clinical data when requested.

Improving Biospecimen Science:

We have isolated RNA and DNA from the metastases from rapid autopsy patients for RNAseq and exome-seq. The exome-seq analyses are ongoing, however the RNAseq analyses in combination with immunohistochemical analyses have provided critical characterization data on castration-resistant specimens from the rapid autopsy program that appear to have lost androgen receptor expression or display neuroendocrine features. 'Phenotyping' the specimens gives the investigator a greater understanding of the specimens they are analyzing enhancing their research.

Impact

One new PDX model was developed. Biospecimens from the clinic, operating room and at autopsy were collected for future use by the prostate cancer research community. Clinical specimens and associated data were provided to researchers.

Changes/Problems

No changes were made to personnel this year. No significant problems were encountered.

Products

The reportable outcomes for the project include tissue acquisition, PDX development, and TMA construction, and specimen distribution are already discussed under accomplishments.

Participants & other Collaborating Organizations

This program involves interactions with the coordinating site at Johns Hopkins for the distribution of specimens.

Special Reporting Requirements

N/A

Appendices

N/A